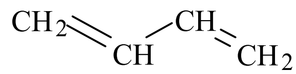
1,3-BUTADIENE
CAS No. 106-99-0

First Listed in the *Fifth Annual Report on Carcinogens* as *Reasonably Anticipated to be a Human Carcinogen* upgraded to *Known to be a Human Carcinogen* in the *Ninth Report on Carcinogens*



CARCINOGENICITY

1,3-Butadiene is *known to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in humans, including epidemiological and mechanistic information, which indicate a causal relationship between occupational exposure to 1,3-butadiene and excess mortality from lymphatic and/or hematopoietic cancers.

In 1989, 1,3-butadiene was first listed in the Fifth Annual Report on Carcinogens as "*reasonably anticipated to be a human carcinogen*" based on evidence of its carcinogenicity in experimental animals. Subsequent to the initial animal cancer findings, 1,3-butadiene has been shown to be metabolized to mutagenic and carcinogenic expoxides (epoxybutene and diepoxybutane) in all mammalian species studied, including humans. In addition, a number of human epidemiology studies have been published including 1) a cohort study showing excess risk for lymphosarcoma and reticulosarcoma in workers who manufactured 1,3-butadiene monomer, 2) a significantly increased risk for leukemia among production workers in a study of styrene-butadiene rubber workers in eight plants in the United States and Canada, and 3) a large excess of leukemia that was associated with exposure to 1,3-butadiene and not to styrene in a case-control study within the cohort of styrene-butadiene rubber workers (reviewed in IARC V 54, 1992). In addition, Ward *et al.* (1996) found an excess of lymphosarcoma and reticulosarcoma among 1,3-butadiene production workers in a previously unstudied chemical plant. Matanoski *et al.* (1993) reported that the standardized mortality ratio for leukemia was 1.8 times higher than that of the U.S. population for long-term workers hired before 1960 who had worked in three of the eight previously studied styrene-butadiene rubber plants. A second case-control study of the lymphopoietic cancers among styrene-butadiene rubber workers (new set of controls per case) confirmed the strong association and significant dose-response effect between increasing 1,3-butadiene exposure score and increasing risk for leukemia (Matanoski et al., 1993). Finally, a follow-up study of styrene-butadiene rubber workers concluded that exposure to 1,3-butadiene in the synthetic rubber industry produced a dose-related increase in the occurrence of leukemia (Macaluso et al., 1996; Delzell et al., 1996).

The evidence that butadiene is a human carcinogen is supported by experimental animal studies which have shown that 1,3-butadiene induces benign and malignant neoplasms at multiple tissue sites in multiple species, and supporting mechanistic data. Experimental studies in laboratory animals demonstrated that 1,3-butadiene is carcinogenic to mice and rats at multiple organ sites. Sites of tumor induction in mice included the hematopoietic system, heart (hemangiosarcomas), lung, forestomach, harderian gland, preputial gland, liver, mammary gland, ovary, and kidney (Huff et al., 1985; Melnick et al., 1990; NTP 288, 1984). Sites of tumor induction in rats included the pancreas, testis, thyroid gland, mammary gland, uterus, and Zymbal gland (Owen et al., 1987).

ADDITIONAL INFORMATION RELEVANT TO CARCINOGENESIS OR POSSIBLE MECHANISMS OF CARCINOGENESIS

Mouse, rat, and human liver microsomes have been shown to oxidize 1,3-butadiene to epoxybutene (Csadány et al., 1992) and further oxidize the monoepoxide to diepoxybutane (Seaton et al., 1995). These metabolites form *N'*-alkylguanine adducts. These adducts have been detected in liver DNA of mice exposed to 1,3-butadiene and identified in the urine of a worker exposed to 1,3-butadiene. Activated K-*ras* genes and inactivated tumor suppresser genes observed in 1,3-butadiene-induced tumors in mice are analogous to genetic alterations frequently observed in a wide variety of human cancers. Dose-related increases in *hprt* mutations have been observed in lymphocytes isolated from mice exposed to 1,3-butadiene or its epoxide metabolites and in occupationally exposed workers. The mutational spectra for 1,3-butadiene and its epoxide metabolites at the *hprt* locus in mouse lymphocytes are similar to the mutational spectrum of ethylene oxide, an alkylating agent classified by IARC as carcinogenic to humans. The mechanism of tumor induction by 1,3-butadiene in rodents and humans appears to be due to its metabolism to DNA-reactive intermediates resulting in genetic alterations in protooncogenes and/or tumor suppressor genes.

PROPERTIES

1,3-Butadiene is a colorless, noncorrosive gas with a mild aromatic or gasoline-like odor. When heated, 1,3-butadiene emits acrid fumes. It is both explosive and flammable, and a dangerous fire hazard when exposed to heat, flame, or powerful oxidizers. When exposed to air, it will also form explosive peroxides that are sensitive to shock or heating above 27 °C, and will explode upon contact with aluminum tetrahydroborate. 1,3-Butadiene is sparingly soluble in water, more soluble in methanol and ethanol, and soluble in most common organic solvents such as acetone, diethyl ether, benzene, and cyclohexane. It readily polymerizes in the presence of sodium or oxygen, and explosive peroxides may form when it is exposed to air (Budavari, 1996; HSDB, 1997; Lewis, 1992). The commercial product is 99% pure. It may contain parts-per-million levels of butadiene dimer (NTP 434, 1993).

Because 1,3-butadiene is a highly volatile gas at room temperature, it is transported to consumers as a liquefied gas under pressure (Morrow, 1990). Means of transportation include pipeline, barge, tank car, and tank truck. During transportation, 1,3-butadiene contains an antioxidant inhibitor such as *tert*-butylcatechol, hydroquinone, or di-*n*-butylamine (Kirshenbaum, 1985).

USE

1,3-Butadiene is used primarily as a chemical intermediate and polymer component in the manufacture of synthetic rubber. Seventy-five percent of 1,3-butadiene produced is used in synthetic rubber manufacture (Morrow, 1990). In 1986, 95% of 1,3-butadiene produced in the United States was used for the production of styrene-butadiene rubber (SBR) (32.7%), polybutadiene rubber (22.3 %), adiponitrile (12.5%), styrene-butadiene latex (9.9%), chloroprene (6.6%), acrylonitrile-butadiene-styrene (ABS) resins (4.4%), nitrile rubber (2.7%), and other uses, including export (3.9%). The major end-use products for most of these copolymers are tires (84% of SBR and 75% of the polybutadiene in North America) and nylon products (adiponitrile) (Kirschner, 1996). Butadiene is also used in the manufacture of the fungicides captan and captafol. The polymers are used in the manufacture of latex adhesives, various rubber products, nylon carpet backings, paper coatings, pipes, conduits, appliance and electrical equipment components, and luggage (SRI, 1982; JACA Corp., 1987).

PRODUCTION

1,3-Butadiene is isolated by distillation or extraction from crude butadiene, which is a by-product of ethylene production. In 1996, 3.8 billion pounds (lb) (1.7 million metric tons or Mg) of 1,3-butadiene was produced, making it the 36th largest chemical product in the United States (Chem. Eng. News, 1997). According to Chemical Market Associates Inc. (Rubber Plast. News, 1997), global 1,3-butadiene consumption is anticipated to increase by 4.1% annually. Projected global production of 1,3-butadiene for the year 2001 is 18.5 billion lb (8.4 million Mg), with North American production being 5.5 billion lb (2.5 million Mg). *Chemical and Engineering News* reported that rubber grade 1,3-butadiene production held steady in 1990 with almost 3.2 billion lb produced domestically (Chem. Eng. News, 1991). This was consistent with annual production figures for the years 1988 and 1989 (USITC, 1989, 1990). This was roughly a 10% increase over the 1987 total of 2.9 billion lb (USITC, 1988, 1989). In 1986, approximately 2.6 million lb of 1,3-butadiene were produced in the United States (USITC, 1987). In 1985, the United States produced over 2.3 billion lb (USITC, 1986). Thirteen domestic manufacturers of 1,3-butadiene produced a total of nearly 2.8 billion lb in 1984 (USITC, 1985). In 1983, over 2.3 billion lb of 1,3-butadiene were produced in the United States (USITC, 1984). U.S. production in 1982 was reported to be nearly 1.9 billion lb (USITC, 1983). In 1981, the United States produced almost 3.0 billion lb (USITC, 1982).

1,3-Butadiene imports exceeded 338 million lb in 1989 (USDOC Imports, 1990). In 1987, the United States imported over 823 million lb of 1,3-butadiene (USDOC Imports, 1987). In 1985, the United States imported 832 million lb and exported over 187 million lb of 1,3-butadiene (USDOC Exports, 1986). In 1984, 158.2 million lb of 1,3-butadiene were exported and 837 million lb were imported (USDOC Exports, 1985). In 1983, 96.5 million lb of 1,3-butadiene were exported and nearly 885 million lb were imported (JACA Corp., 1987; Chem. Week, 1984b). In 1982, imports of 1,3-butadiene were 867.7 million lb, and exports were 102.5 million lb (Chem. Week, 1984b). In 1981, the United States imported nearly 458 million lb and exported 122 million lb of 1,3-butadiene (SRI, 1982).

EXPOSURE

The primary routes of potential human exposure to 1,3-butadiene are inhalation, ingestion, and dermal contact. Manufacturing, transporting, or using 1,3-butadiene are among the major anthropogenic sources of 1,3-butadiene releases to the environment (ATSDR, 1992-H009; Eastern Research Group, USA, 1996). Sources of 1,3-butadiene emissions include facilities producing 1,3-butadiene, styrene-butadiene copolymer, polybutadiene, neoprene, acrylonitrile-butadiene-styrene (ABS) copolymer, nitrile elastomer, and adiponitrile. Lesser emissions are discharged by facilities producing styrene-butadiene-vinylpyridine (SBV) latex, butadiene-vinylpyridine latex, tetrahydrophthalic anhydride, captan, captafol, 1,4-hexadiene, dodecanoic acid, butadiene dimers, methyl methacrylate-[acrylonitrile]-butadiene-styrene resins, ethylidene norbornene, butadiene-furfural cotrimer, sulfolane, and 1,3-butadiene cylinders, and poly(vinyl chloride. Because 1,3-butadiene is an impurity at 6 ppm in vinyl chloride monomer, 1,3-butadiene emissions of 210 µg per kilogram poly (vinyl chloride) (PVC) have been estimated for PVC production (Eastern Research Group, USA, 1996).

Occupational exposure to 1,3-butadiene may occur through inhalation and, to a lesser extent, dermal contact (NTP 288, 1984). The National Occupational Exposure Survey (NOES) conducted by the National Institute for Occupational Safety and Health (NIOSH) for 1981-1983 estimated that 51,971 total workers, including 1,411 women, at 2,201 facilities were potentially exposed to 1,3-butadiene (NIOSH, 1990). The National Occupational Hazard Survey (NOHS), conducted by NIOSH from 1972 to 1974, estimated that 69,555 workers were potentially exposed to 1,3-butadiene in the workplace (NIOSH, 1976). The NOHS indicated that 44,980 workers (69% of the total number of workers potentially exposed) were employed in the chemical and allied products industry; 9,086 workers (14%) were employed in the rubber and plastics products industry; 5,339 workers (8%) were employed in miscellaneous business services; and 2,244 workers (3.4%) were employed in various manufacturing industries (NIOSH 41, 1984). Health Hazard Evaluation surveys conducted by NIOSH at six facilities indicated that exposures to 1,3-butadiene in those facilities were significantly below the 1984 OSHA permissible exposure limit (PEL) of 1,000 ppm as an 8-hr time-weighted average (TWA). The range of reported exposures was 0.06 to 39 ppm. The types of facilities surveyed included those which manufactured helmets and visors, synthetic rubber, rubber tires and tubes, automotive weather stripping, braided hoses, and plastic components for aircraft (NIOSH, 1984). The ACGIH recommended threshold limit value (TLV) for 1,3-butadiene as an 8-hr TWA is 2 ppm (ACGIH, 1996).

Osterman-Golkar *et al.* (1996) monitored (using stationary and personal monitoring) 17 workers in the 1,3-butadiene production unit in a Swedish petrochemical plant to determine workplace exposure. Average exposure for workers handling 1,3-butadiene containers was 11.2 $\pm$ 18.6 mg/m^3 (5.06 $\pm$ 8.41 ppm). Maintenance and laboratory workers exposure was 1.2 mg/m^3 (0.54 ppm). These concentrations were determined by analyses of personal and area full shift air sample.

NIOSH conducted studies to determine 1,3-butadiene exposure in monomer, polymer, and end-user industries. Workers in 5 job areas were classified as having potentially higher exposure to 1,3-butadiene. These 5 areas included maintenance technician (0.026 - 94.38 mg/m^3; 0.012 - 42.7 ppm), loading (0.17 - 273 mg/m^3; 0.08 - 123 ppm), tank farm (0.02 - 52.8 mg/m^3; 0.009 - 24 ppm), process (i.e., purification, polymerization, and reaction) (< 0.011 - 76.78 mg/m^3; < 0.0050 - 34.7 ppm), and laboratory (< 0.0132 - 822.8 mg/m^3; < 0.006 - 372 ppm). Exposure concentrations were determined from personal or area full-shift air samples. Exposure of workers in the monomer industry, based on personal full-shift and short-term air samples (including subcategories of laboratory technician and process technician), ranged from < 0.02 to 374 ppm (< 0.04 - 827 mg/m^3). Personal exposure of workers in the polymer industry (including laboratory technician, tank farm operator, front end [reaction], maintenance technician, and back end [finishing]) ranged from < 0.005 to 42.9 ppm (< 0.01 - 94.9 mg/m^3) for full-shift samples and 0.087 to 280 ppm for short-term exposures. Full-shift (0.19 to 619 mg/m^3) area air samples in the polymer industry indicated 1,3-butadiene exposure ranging from less than 0.006 to 9.01 ppm (< 0.01 - 19.9 mg/m^3). For the monomer industry as a whole, 1,3-butadiene concentrations were > 10 ppm (22 mg/m^3) in 7.1% of the samples, 2-10 ppm (4 to 22 mg/m^3) in 12.8%, 1-2 ppm (2 - 4 mg/m^3) in 12.3% and < 1 ppm in 67.8% (the present OSHA permissible limit is 1 ppm). For the polymer industry as a whole, the corresponding percentages for these 4 ranges were 3.3%, 7.7%, 3.3%, and 85.8%, respectively. The arithmetic mean exposure for personal full-shift exposures in the polymer plants was 1.14 ppm (2.57 mg/m^3) (Fajen et al., 1993).

Of 184 facilities reporting on 1,3-butadiene emissions to the U.S. EPA for the 1995 Toxic Chemical Release Inventory, 175 reported a total of 2,913,561 lb of 1,3-butadiene released to air. Total nonpoint air emissions were 1,437,468 lb from the 169 facilities reporting nonpoint air emissions such as process venting and equipment leaks (TRI95, 1997). TRI95 (1997) reported releases of 1,3-butadiene to surface water totaling 5,398 lb, while a total of 277 lb of 1,3-butadiene was released to land in 1995. The Toxic Chemical Release Inventory listed 145 industrial facilities that produced, processed, or otherwise used 1,3-butadiene in 1988 (TRI, 1990). In compliance with the Community Right-to-Know Program, the facilities reported releases of 1,3-butadiene to the environment which were estimated to total 68 million lb.

A nationwide 1,3-butadiene inventory (including vehicle emissions and emissions from manufacturing and producing facilities) calculated annual butadiene emissions to air to be 102,000 Mg/yr for the year 1990 (Ligocki et al., 1994), considerably higher than the TRI 1990 reports of 2294 Mg/yr for industrial emissions. Calculations were based on butadiene emission factors for the various emission sources considered.

1,3-Butadiene is emitted from furnaces at secondary lead smelting facilities handling automotive lead-acid batteries that contain plastic battery separators or that have hard rubber casings. In 1992, petroleum refineries were the fourth largest emitters of 1,3-butadiene with 1,3-butadiene being released from blowdown vents; catalyst regeneration process vents; and miscellaneous vents at vacuum distillation, alkylation, and thermal cracking units (Eastern Research Group, USA, 1996).

Volatilization of 1,3-butadiene from wastewaters of styrene-1,3-butadiene copolymer production at publicly owned treatment works (POTW) has been calculated to be 21 tons/yr (19 Mg/yr) (Eastern Research Group, USA, 1996).

1,3-Butadiene is naturally formed as a byproduct of forest fires (HSDB, 1997). Emissions from wood burning in a wood-stove and small-scale model experiments showed that 1 to 2% by weight of total nonmethane hydrocarbons emitted were 1,3-butadiene (Barrefors and Peterson, 1995).

Incomplete combustion of a variety of fuels forms 1,3-butadiene as a product. 1,3-Butadiene comprises 0.5 to 2 % of the total organic gas emissions from most types of combustion (Ligocki et al., 1994). It can also be found in exhaust emissions from motor vehicles as a product of incomplete combustion of gasoline and diesel oil and from the thermal breakdown of plastics (ATSDR, 1992-H009; Eastern Research Group, USA, 1996).

California has run dispersion modeling from a typical freeway source and has estimated that gasoline-fueled vehicles emit 0.011g/mi (Cooper and Reisman, 1992). Ligocki et al. (1995a) calculated that onroad gasoline vehicle exhaust contained 0.59% 1,3-butadiene by weight. Diesel vehicle exhaust contained 1.55% 1,3-butadiene by weight.

Cigarette smoke is also an environmental source of 1,3-butadiene. Releases into the air in sidestream smoke have been variously estimated at 152 to 400 µg 1,3-butadiene per cigarette (Ligocki et al., 1995b). Calculations based on 400 µg/cigarette indicate that 1,3-butadiene concentrations in the homes of smokers would be increased by about 4 $\mu g/m^3$, and concentrations in air at workplaces allowing smoking would increase by 13 $\mu g/m^3$ (Wallace, 1991).

Certain cooking oils release 1,3-butadiene when heated. For example, 1,3-butadiene emissions were approximately 22-fold higher from heated unrefined Chinese rapeseed oil than from heated peanut oil. Of three fatty acids tested, heated linolenic acid produced the greatest amount of 1,3-butadiene. Although cooking oils in the United States are refined for purity, U.S. rapeseed oil (canola) also emitted 1,3-butadiene (Shields et al., 1995).

The Chemical Manufacturers Association (CMA) studied baseline VOC measurements in Washington, D. C., from March 12, 1990, to March 11, 1991. 1,3-Butadiene was detected in 26.79% of the samples collected for 24-hour periods, once every 6 days. Preliminary results indicated a mean 1,3-butadiene concentration of 0.13 ± 0.17 ppb (0.29 ± 0.38 $\mu g/m^3$). The maximum concentration observed was 0.83 ppb (1.8 $\mu g/m^3$). The mean was calculated using randomly generated values between zero and the detection limit for all samples in which butadiene was below the limit of detection. Washington, D.C., was selected since it was one of the largest cities that did not contain large industrial air pollution sources (Hendler and Crow, 1992).

Outdoor 1,3-butadiene concentrations in six United States urban settings were in the range 0.3 - 1.6 $\mu g/m^3$ (0.14 - 0.72 ppbv) (Wallace, 1991). California's statewide population-weighted exposure to ambient (outdoor) airborne 1,3-butadiene was estimated to be an average of 0.37 ppb (0.82 $\mu g/m^3$). One-hour outdoor concentrations ranged to a high of 17.7 ppb (39.1 $\mu g/m^3$). Similar indoor concentrations were observed in taverns where heavy smoking conditions existed (Seiber, 1996).

Additional exposure information is presented in other available documents (ATSDR, 1992-H009; Eastern Research Group, USA, 1996).

REGULATIONS

EPA regulates 1,3-butadiene under the Clean Air Act (CAA), the Toxic Substances Control Act (TSCA), the Resource Conservation and Recovery Act (RCRA), and the Superfund Amendment and Reauthorization Act (SARA). 1,3-Butadiene is listed as a hazardous air pollutant, and emission standards have been established under the CAA. It is subject to the submission of information relating to the release of toxic chemicals under Section 313 of Title III of SARA (1986), and health and safety data reporting under TSCA. The Superfund (CERCLA, SARA) reportable quantity (RQ) for 1,3-butadiene is 1 lb. Notification of EPA is required if the RQ is released to the environment. FDA regulates 1,3-butadiene as an indirect food additive.

NIOSH recommends that the exposure limit of the compound be the lowest feasible concentration (NIOSHc, 1994). OSHA has lowered the PEL for 1,3-butadiene from 1000 ppm to 1 ppm as an 8-hr TWA, with a 15-minute short-term exposure limit (STEL) of 5 ppm. Prior to 1996, OSHA regulated 1,3-butadiene exposure with a PEL of ≤ 1,000 ppm as an 8-hr TWA. OSHA also regulated 1,3-butadiene under the Hazard Communication Standard and as a chemical hazard in laboratories. OSHA also regulates 1,3-butadiene under the Hazard Communication Standard and as a hazardous chemical in laboratories. Regulations are summarized in Volume II, Table A-11.